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REMARKS

The Applicants respectfully request reconsideration of this application in view of the above amendments and the following remarks.

**35 U.S.C. §112 Rejection, Second Paragraph**

Claims 10-14 and 22-29 are rejected under 35 U.S.C. 112, second paragraph.

This rejection is believed to be moot in view of the amendments above.

**35 U.S.C. §101/112-1 Rejection**

Claims 10-14 and 22-29 are rejected under 35 U.S.C. 101.

An asserted utility is determining a three-dimensional protein structure. See e.g., original claim 10. The Examiner has relied upon Orengo and Russel to show that prediction of protein structure is difficult and uncertain. The Examiner has based on this asserted that further research would be required to determine whether the structures determined according to the present patent application has any relevance to real world native structures.

Initially, as discussed in MPEP 2107.01.I.C, "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., that they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense". Applicants respectfully submit that the presently claimed method likewise has a clear, specific and unquestionable utility (e.g., that they are useful in analyzing proteins). The fact that determining protein structure tends to be difficult does not negate this. As discussed in paragraphs [0003] and [0004] of the patent application, X-ray crystallography and NMR likewise at times have difficulties determining protein structure. It seems that an extension of the Examiner's reasoning would attempt to lead

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one to the erroneous conclusion that such X-ray and NMR systems also would not have utility, which naturally is incorrect.

Accordingly, at least one utility determining a three-dimensional protein structure. This one utility alone is sufficient to satisfy the utility requirement.

Furthermore, as understood by Applicants, Orengo's comment pertains to particular ab initio approaches and should not be taken out of context. Furthermore, Orengo doesn't indicate that the ab initio approaches never work. In particular, as evident from Orengo's Figure 1, the techniques seemingly work much better for easy targets. One example of extremely easy targets would be extremely small proteins. Applicants respectfully submit that the techniques disclosed in the present patent application should be sufficient to determine the three-dimensional protein structure of such extremely small proteins that no further research would be required to determine whether the structures determined according to the present patent application has any relevance to real world native structures. Neither Orengo's or Russel's statements refute this understanding. Accordingly, at least one utility of the presently claimed invention is determining a three-dimensional protein structure for an extremely small protein. This one utility alone is sufficient to satisfy the utility requirement.

Another asserted utility of the determined three-dimensional protein structures is for design of novel drugs. See e.g., paragraph [0002]. A further utility lies in using the determined structures for extremely small proteins for design of novel drugs.

Yet another asserted utility of the determined three-dimensional protein structures is for design of synthetic proteins of specified function. See e.g., paragraph [0002]. A further utility lies in using the determined structures for extremely small proteins for design of synthetic proteins of specified function.

A well established utility is displaying a determined three dimensional protein structure on a display device for education, learning, research, or drug design purposes. It is well established in that certain computer programs that predicted structure at the time

the invention was made allowed structures to be displayed. A further utility lies in displaying structures of extremely small proteins.

United States Patent 5,878,373 discloses comparing proteins or determining the topological similarities between structurally dissimilar proteins. The '373 patent also discloses screening techniques for determining protein sequences that have a structure similar or homologous to the structure of a known sequence. Accordingly, other well established utilities of the determined three-dimensional protein structures are for such comparisons or for determine topological similarities between structurally dissimilar proteins. Further well established utilities of the determined three-dimensional protein structures are for such screening techniques. Yet further utilities are corresponding utilities but for extremely small proteins.

United States Patent 5,842,151 discloses that the tertiary structure of a receptor protein is useful when a docking simulation is performed on a molecule of drug and an active site of the protein. Such a simulation is performed to investigate as to which part of a sequence of residues, which is a sequence of molecules of the protein, will be docking with the drug. If the tertiary structure is known, the drug design will be possible. See e.g., the Background section. Accordingly, other well established utilities of the determined three-dimensional protein structures is to allow a docking simulation to be performed. Another well established utilities of the determined three-dimensional protein structures are to facilitate or allow drug design. Yet further utilities are corresponding utilities but for extremely small proteins.

United States Patent 6,377,893 discloses methods of excluding homology between two protein families including generating as a useful and practical result the statement of condition that the two families might be related by common ancestry or are not. See e.g., claim 1. Accordingly, yet another well established utility of the determined three-dimensional protein structures is to be used as a tool to rule out long distance homology of proteins. A further utility lies in applying this to extremely small proteins.

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Another well established utility is to quickly and/or economically eliminate certain relatively less relevant proteins from a list of candidate proteins based on the determined three-dimensional protein structures so that costly and/or time consuming study need not be expended on them. Yet another well established utility is to quickly and/or economically select relatively more relevant proteins from a list of candidate proteins for further study. A further utility lies in applying this to extremely small proteins.

Accordingly, the presently claimed inventions each have at least one utility. Accordingly, the rejection should be withdrawn.

#### **35 U.S.C. §112 Rejection**

Claims 10-14 and 22-29 are rejected under 35 U.S.C. 112, first paragraph.

This rejection is believed to be moot in view of the amendments and remarks above.

#### **35 U.S.C. §101 Rejection**

Claims 10-14 and 22-29 are rejected under 35 U.S.C. 101.

This rejection is believed to be moot in view of the amendments and remarks above.

#### **35 U.S.C. §103(a) Rejection – Monge, Freisner, Russell, Andricioaei and Zhou**

The Examiner has rejected claims 10-14 and 22-29 under 35 U.S.C. §103(a) as being unpatentable over Monge et al. (Proc. Natl. Acad. Sci, 1994, 91, 5027-5029) (hereinafter referred to as "Monge") or Freisner et al. (US Patent No. 5,600,571) (hereinafter referred to as "Freisner") or Russell et al. ("A Guide to Structure Prediction", <http://www.russell.embl-heidelberg.de/gtsp/index.html>) (hereinafter referred to as "Russell") in view of Andricioaei (Journal of Chemical Physics, 04/2001, Vol.114 (16), pp. 6994-7000) (hereinafter referred to as "Andricioaei") or Zhou et al. (The Journal of Chemical Physics, 1997, 107, 9185-91 960) (hereinafter referred to as "Zhou").

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The Applicants respectfully submit that the present claims are allowable over any combination of Monge, Freisner, Russell, Andricioaei and Zhou.

Without admitting that these references should be combined, Applicants respectfully submit that the rejection is moot in view of the amendments above. In particular, the rejection is moot in view of the amendment to delete "smart moves" and add "wherein adjusting the dihedral angles is based on the secondary structure".

**35 U.S.C. §103(a) Rejection – Monge, Freisner, Russell, Andricioaei, Zhou, Evans  
Debe and Sadanobu**

The Examiner has rejected claims 11-14 and 22-29 under 35 U.S.C. §103(a) as being unpatentable over Monge, Freisner, Russell, Andricioaei and Zhou and further in view of Evans et al. (Protein Science, 1995, 4, 1203-1216) (hereinafter "Evans"), and Debe et al. (Proc. Natl Acad. Sci., 1999, 96, 2596-2601) (hereinafter referred to as ("Debe")) and Sadanobu et al. (J. Chem. Phys. 106:6722, 1997) (hereinafter referred to as "Sadanobu").

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully submit that these references should not be combined. There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. The Examiner has failed to provide a suggestion or motivation for the combination of these references. Accordingly, the rejection of these claims should be withdrawn.

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**Conclusion**

In view of the foregoing, it is believed that all claims now pending patentably define the subject invention over the prior art of record and are in condition for allowance. Applicants respectfully request that the rejections be withdrawn and the claims be allowed at the earliest possible date.

**Request For Telephone Interview**

The Examiner is invited to call Brent E. Vecchia at (303) 740-1980 if there remains any issue with allowance of the case.

**Request For An Extension Of Time**

The Applicants respectfully petition for an extension of time to respond to the outstanding Office Action pursuant to 37 C.F.R. § 1.136(a) should one be necessary. Please charge our Deposit Account No. 02-2666 to cover the necessary fee under 37 C.F.R. § 1.17 for such an extension.

**Charge Our Deposit Account**

Please charge any shortage to our Deposit Account No. 02-2666.

Respectfully submitted,

BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN LLP

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